

REMARKS

Status of the Claims

Claims 1-7, 9, 10 and 14 are pending. Claims 1-7, 9, 10 and 14 are rejected.

Claims 1, 2, 3, 4, 5, 6, 7 and 14 are amended and claims 9 and 10 are canceled herein. No new matter is added to these claims.

Claim amendments

Claim 1 is amended to overcome the 35 U.S.C. §102(b), §103(a) and 35 U.S.C. §112, second paragraph rejections. Amended claim 1 is drawn to a mouse/human chimeric anti-phencyclidine (PCP) monoclonal antibody. Such an antibody comprises a full-length chimeric heavy chain and a full-length chimeric light chain. The sequence of the full-length chimeric heavy chain comprises a leader sequence of a heavy chain of a murine antibody, a variable domain sequence of the heavy chain of the murine antibody and a human immunoglobulin heavy chain constant domain sequence. The sequence of the full-length chimeric light chain comprises a leader sequence of a light chain of a murine antibody, a variable domain sequence of the light chain of the murine antibody and a human immunoglobulin light chain constant domain sequence (Figs. 9, 10, 11A-11B; pg 24, lines 10-16; pg 24, line 27-pg. 25, line 17).

Claims 4-7 are amended so that they are no longer open-ended and properly depend from amended claim 1. Accordingly, amended claims 4

and 5 limit the amino acid and DNA sequence of the full-length chimeric light chain to SEQ ID No: 16 and 15 of the mouse/human chimeric anti-phencyclidine monoclonal antibody, respectively. Similarly, amended claims 6 and 7 limit the amino acid and DNA sequence of the full-length chimeric heavy chain to SEQ ID No: 18 and 17 mouse/human chimeric anti-phencyclidine monoclonal antibody, respectively. Additionally, claims 2, 3 and 14 are amended so that they properly depend from the amended claim 1.

The 35 U.S.C. §102 Rejection

Claims 1-3 and 14 stand rejected under 35 U.S.C. §102(b) as being anticipated by **U.S. Patent No. 6,358,710 B1**. Applicant respectfully traverses this rejection.

The Examiner disagrees with Applicant's argument that **U.S. Patent No. 6,358,710** did not teach all limitations of the claims since it did not teach the leader sequences in the chimeric mouse/human monoclonal antibody for the following reason. **U.S. Patent No. 6,358,710** teaches the chimeric mouse/human monoclonal antibody comprising the human constant heavy and light chains and murine variable heavy and light chain region (col. 10, lines 18-27, in particular). Additionally, **U.S. Patent No. 6,358,710** teaches the use of a signal peptide in expressing the recombinant antibodies in cell culture (col. 23-24). Furthermore, the inclusion of the leader sequence in claim 1 does not obviate this rejection because the leader sequence is not part of a purified

antibody form since the specification of the instant invention teaches that the leader sequence is to be removed from the polypeptide upon entry into ER. Based on this, the Examiner maintains that the prior art teachings anticipate the claimed invention. Applicants respectfully disagree.

Claim 1 is amended to recite the components of the mouse/human chimeric anti-phencyclidine monoclonal antibody as discussed supra. The instant invention is drawn to a genetically engineered chimeric anti-PCP monoclonal antibody (page 5, lines 21-24). With regard to this, the instant specification discloses a "full-length" chimeric heavy chain and a "full-length" chimeric light chain of the antibody. This "full-length" chimeric heavy or light chain comprises a leader sequence of the murine heavy chain or a leader sequence of the murine light chain, respectively. This leader sequence precedes the variable domain sequence of the heavy chain of the murine antibody and a human immunoglobulin heavy chain constant domain sequence in a full-length chimeric heavy chain. Similarly, the leader sequence precedes the variable domain sequence of the light chain of the murine antibody and a human immunoglobulin light chain constant domain sequence in a full-length chimeric light chain. (pg 24, lines 10-16; pg 24, line 27-pg. 25, line 17; Figs. 9, 10, 11A, 11B). Hence, the amendments made to claim 1 are supported by the teachings of the instant specification.

Further, Applicant disagrees with the Examiner's contention that since the leader sequence is not part of a purified antibody form, its inclusion does not obviate the rejection. The instant claim is drawn to a chimeric anti-

phencyclidine antibody. As disclosed in the instant specification, the instantly claimed antibody was generated by cloning of the cDNA of mAb6B5 V_L and V_H including their respective leader sequences. The instant specification emphasizes the need to include the leader sequence by stating that such an inclusion would ensure proper assembly and secretion of the chimeric mAb6B5. In fact, the sequences shown in SEQ ID No: 15, 16, 17 and 18 and claimed herein comprise the leader sequences (Figs. 10, 11A, 11B). Hence, Applicant submits that the leader sequence should be included in the chimeric mouse/human monoclonal antibody that comprises "full-length" chimeric heavy chain and "full-length" chimeric light chain.

In contrast to the teachings of the instant invention, **U.S. Patent NO: 6,358,710** teaches generation of a humanized antibody that targets human cancer antigen, which is a glycoprotein that is expressed on most carcinomas (Background of the Invention). In this regards, the prior art teaches generation of a humanized antibody that binds to the same antigens as is bound by NR-LU-13 (Summary of the Invention). Thus, **U.S. Patent NO: 6,358,710** does not teach generation of a mouse/human chimeric anti-phencyclidine monoclonal antibody. Additionally, **U.S. Patent NO: 6,358,710** does not teach of the components of the full-length chimeric heavy chain and the full-length chimeric light chain as recited in the instant claim 1.

In order to anticipate a claim, the prior art reference must teach all elements of the instant claim. As discussed herein, **U.S. Patent No. 6,358,710** does not teach all elements of claim 1 and thus, cannot anticipate claim 1. Since

claim 14 is dependent from the amended claim 1, it is also not anticipated by the prior U.S. Patent NO: 6,358,710. Accordingly, based on the claim amendments and the remarks herein, Applicant respectfully requests the withdrawal of rejection of claims 1-3 and 14 under 35 U.S.C. §102(b).

The 35 U.S.C. §103 Rejection

Claims 1-10 and 14 stand rejected under 35 U.S.C. §103(a) as being unpatentable over **Hardin et al** (J Pharm Exp Ther., 285:1113-1122, 1998) as is evidenced by **Lim et al** (J Biol Chem, 273(44): 28576-28582, 1998) and U.S. Patent No. 6,358,710 in view of **McLean et al** (Mol Imm 37:837-845, 2000). Applicant respectfully traverses this rejection.

The Examiner held Applicant's arguments unpersuasive because the leader sequence is not a part of the purified form of an antibody as discussed supra. The Examiner reiterates the teachings of cited prior art references as follows. **Hardin et al** teach the murine monoclonal antibody mAb6B5 Fab (abstract, p. 1114 under Materials and Methods) binds to phencyclidine and **Lim et al** disclose the complete sequences of mAb6B5 heavy chain and light chain (fig. 1). According to the Examiner, it is well-known in the antibody therapy art to develop a humanized antibody to reduce immunogenicity (U.S. Patent No. 6,358,710, col. 1, lines 35-50). Further, although **Hardin et al** do not teach chimeric murine and human antibodies, **McLean et al** teach various human expression vectors associated with IgG1, IgG2, IgG3, IgG4 and kappa chain constant regions. These expression vectors are constructed to include promoter sequences, leader

sequences (2.3-2.5, Fig. 1, 2), drug resistant marker and VDJ cassette, which can be replaced with any variable region of interest (p. 841, 2.7). Additionally, these expression vectors are easy to manipulate by replacing various variable regions (i.e. Fab of mAb6B5) to produce functional Ig proteins (p. 843, 3.3) and can be used in transfection to generate Ig antibodies (2.5). Therefore, the Examiner concludes that one of ordinary skill in the art would have been motivated to combine the variable region of murine mAb6B5 Fab taught by *Hardin et al* and *Lim et al* in the expression cassette with built in human constant heavy and light chain regions taught by *McLean et al* to create therapeutically more important chimeric antibody and produce functional Ig. Applicants respectfully disagree.

Claim 1 has been amended as discussed supra and recites a "full-length" chimeric heavy chain and a "full-length" chimeric light chain of a mouse/human chimeric anti-phencyclidine monoclonal antibody that includes a leader sequence. This amendment is supported by the teachings of the instant invention as discussed supra. The cited prior art references combined do not teach or suggest a full-length chimeric heavy chain or a full length chimeric light as taught by the instant invention. This is substantiated by comparing the heavy chain and light chain variable regions of the antibody taught in *Lim et al* (Fig. 1). The sequence disclosed in *Lim et al* differs from the sequence disclosed in the instant invention. Thus, the prior art references combined do not teach or suggest all claim limitations.

Additionally, the instant specification discloses a lack of knowledge of the sequence (leader sequence through the J-C junction) required to amplify the appropriate sequence of each chain (page 24, line 27-page 25, line 1). Hence, Applicant submits that even if one of ordinary skill in the art were motivated to combine the teachings of the prior art references as suggested by the Examiner, one would be randomly experimenting in an attempt to arrive at the instantly claimed monoclonal antibody in the absence of teachings of the instant invention. Thus, the invention as a whole was not prima facie obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, based on the claim amendments and remarks, Applicant respectfully requests the withdrawal of rejection of claims 1-10 and 14 under 35 U.S.C. §103(a).

The 35 U.S.C. §112, Second Paragraph Rejections

Claims 1-7, 9, 10 and 14 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Applicant respectfully traverses this rejection.

The Examiner states that claims 9-10 are indefinite since they are dependent upon a canceled claim. Claims 9 and 10 are canceled herein. Hence, the rejection of these claims is moot.

The Examiner further states that claim 1 is indefinite in its recitation of a leader sequence since this sequence is to be removed from the polypeptide

upon entry to ER. Thus, the leader sequence will not be present in the final purified antibody.

As discussed supra, claim 1 is amended to recite a full-length chimeric heavy chain and a full-length chimeric light chain. The instant invention teaches that the full-length chimeric heavy chain and a full-length chimeric light chain includes a leader sequence as discussed supra. In fact, the full-length chimeric heavy chain and a full-length chimeric light chain sequences claimed herein comprise a leader sequence. Hence, amended claim 1 is not indefinite. Accordingly, based on the claim amendments and remarks, Applicant respectfully requests the withdrawal of rejection of claims 1-7 and 14 under 35 U.S.C. §112, second paragraph.

The 35 U.S.C. §102(b) Rejection

Claims 1-7, 9, 10 and 14 are rejected under 35 U.S.C. §102(b) as being anticipated by the U.S. Patent No. 6,358,710 B1. Applicant respectfully traverses this rejection.

The Examiner states that U.S. Patent No. 6,358,710 teaches a chimeric antibody derived from a monoclonal antibody of human and murine origins (col. 7, lines 4-25). The Examiner further states that U.S. Patent No. 6,358,710 teaches the use of human constant regions of IgG2, IgG4 as heavy chain and kappa for light chain, respectively (col. 7, lines 10-15) and administering the antibody with drugs or clearing agent (col. 8, lines 46-67).

Additionally, the Examiner states that **U.S. Patent No. 6,358,710** teaches that the use of a leader sequence (e.g. signal peptide) in expressing the recombinant antibodies in cell culture (col. 23-24 overlapping paragraph, in particular) and expression vectors (col. 22-24).

Furthermore, the Examiner states that claims 4 and 6 are currently amended to an antibody "has an amino acid sequence of SEQ ID NO: 16 and SEQ ID NO: 18". Thus, the claims encompass any chimeric antibodies comprising any "portion" of SEQ ID NO: 16 or 18 and thus, anticipate any dipeptide or larger peptide. The Examiner further states that **U.S. Patent No. 6,358,710** recites use of IgG2 and kappa constant region which correspond to amino acids 130-462 of SEQ ID NO: 18 and amino acids 130-237 of SEQ ID NO: 16, respectively. Based on this, the Examiner states that **U.S. Patent No. 6,358,710** anticipates the claimed invention. Applicants respectfully disagree.

Claim 1 is amended as discussed supra. Amended claims 1 and 14 are not anticipated by **U.S. Patent No. 6,358,710 B1** (*see discussion supra*). Additionally, claims 4, 5, 6, 7 are amended so that they are no-longer open-ended and recite definite sequences. Thus, the claims encompass antibodies that consists of the entire sequence of SEQ ID NO: 15, 16, 17 and 18.

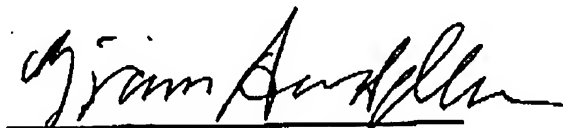
In order to anticipate a claim, the prior art reference must teach and every element of the claim. Since **U.S. Patent No. 6,358,710 B1** teaches only a part of the sequence, this prior art reference does not anticipate the claimed invention. Accordingly, based on the claim amendments and remarks, Applicant

respectfully requests the withdrawal of rejection of claims 1-7, 9, 10 and 14 under 35 U.S.C. §102(b).

This is intended to be a complete response to the Final Office Action mailed October 24, 2006. Applicant submits that the pending claims are in condition for allowance. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: Jan 24, 2007



Benjamin Aaron Adler, Ph.D., J.D.
Registration No. 35,423
Counsel for Applicant

ADLER & ASSOCIATES
8011 Candle Lane
Houston, Texas 77071
(713) 270-5391 (tel.)
(713) 270-5361 (fax.)
badler1@houston.rr.com